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## PATHOLOGY OF AMEBIASIS\*

FIDELIO JIMENEZ, M.D.

Chief of Pathology and Laboratory Services  
Veterans Administration Medical Center  
Brooklyn, New York

THIS review of the pathology of amebiasis is confined to changes encountered in tissues parasitized by these protozoa. The morphology of the parasites and their mechanism of infestation are not included because they are discussed elsewhere in this symposium.

*E. histolytica* is primarily a lumen-dwelling protozoa of the large intestine. After ingestion of an amebic cyst, the trophozoites excyst in the small intestine and, while in suspension in the intestinal contents, are carried to the large intestine where the amebas proliferate and invade the wall. Whether or not amebas can live in the lumen of the large intestine as commensals is a matter of dispute. The intestinal lesions produced by *E. histolytica* are primarily located in the large intestine except for a few in the terminal ileum (Table I). Any segment of the large intestine has served as primary site, but initial lesions are more frequently encountered in those areas where the colonic flow is slow, namely, the cecum and rectosigmoid. The frequency of involvement of the various colonic segments is illustrated in Table I.

The gross appearance of intestinal amebiasis is extremely variable due to the influence of diet, bacterial flora, secondary infections, etc.; thus, to detail all the nuances of the gross presentations would be tiresome and impractical. The initial lesion is a pinhead sized, nonulcerated, nodular elevation of mucosal edema and erythema which rapidly progresses to central ulceration. This ulceration is confined to the mucosal epithelium and lamina propria and does not extend deep to the muscularis mucosa. As the disease process continues, the ameba reaches the submucosa and the ulcer increases in size and depth. When the ulcers reach the muscularis propria they extend laterally along the axis of the intestine undermining

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\*Presented as part of a *Symposium on Amebiasis: A New Look at an Old Disease* presented by the Committee on Public Health of the New York Academy of Medicine October 29, 1980.

Address for reprint requests: 340 East 64th Street, New York, N.Y. 10021

TABLE I. INTESTINAL LESIONS IN 148 CASES

<i>Location of principal involvement</i>	<i>Distribution</i>		<i>Perforation number</i>
	<i>Number</i>	<i>Percent</i>	
Entire colon (multiple)	60	40.5	9
Cecum and terminal ileum	7	4.7	—
Cecum alone	21	14.2	19
Appendix	0	0.0	2
Cecum, ascending colon	14	9.5	—
Ascending colon	6	4.1	4
Transverse and descending colon	4	2.7	7
Rectosigmoid	11	7.4	5
Subtotal	123	83.1	46

the overlying mucosa, which appears grossly normal. The communication of these laterally spreading ulcers with the intestinal lumen through a narrow mucosal defect creates the so called "flasklike" ulcers. Adjacent ulcers may coalesce, leading to larger mucosal defects covered by a greenish-yellow to dark-brown slough composed of fibrin, blood, and cellular debris. The floor of the ulcer may contain remnants of more resistant stroma which project into the lumen as anemonelike tendrils. In advanced cases, ulcers extend beyond the muscularis propria. In those instances, intestinal contents are separated from the peritoneal cavity only by a greenish-yellow to dark-brown edematous serosa that may tear readily when manipulated either during surgery or at autopsy. Spontaneous perforations of the intestine occur most frequently in the cecum (Table I). These perforations can communicate either with the peritoneal cavity, the retroperitoneal space, or with another viscus. On microscopic examination an established amebic ulcer shows irregular areas of necrosis of mucosa and submucosa. The trophozoites are found at the base of the ulcer or in the adjacent, less involved tissues. It should be emphasized that the usual evidence of inflammation other than edema and hyperemia is frequently absent unless there is an accompanying secondary bacterial infection. Amebas may also be found on the mucosal surface within an exudate composed of fibrin, mucus cellular debris, and inflammatory cells.

A relatively rare form of colonic amebiasis is an ameboma which in essence is an exaggeration of the usual findings in chronic amebiasis, namely, more pronounced edema, exuberant growth of granulation tissue,

and marked fibroblastic proliferation. The inflammatory infiltrate may contain large numbers of eosinophils. The thickened wall of the amebomas produces segmental narrowing of the intestinal lumen which radiologically and on gross inspection may easily be mistaken for carcinoma. Amebomas are more frequently located in the rectum and cecum.<sup>2</sup>

#### AMEBIC ABSCESS OF THE LIVER

This is the most important of the extraintestinal complications of amebiasis both because of its frequency and somber prognosis. These abscesses are most frequently located in the right lobe, can be single or multiple, and may attain enormous size. Macroscopically, an early abscess is represented by a small area of parenchymal liver cell necrosis with an amorphous, tan-to-grayish-brown cut surface. As the area of necrosis increases in size, the center liquifies and a true cavity forms. The contents, which are sterile and nonpyogenic, become viscid and chocolate-colored ("anchovy paste") with flakes of more solid tissue. Following evacuation of the contents, the inner surface of the cavity presents a shaggy, fibrinous lining bridged by remnants of more resistant necrotic tissues. Amebas are infrequently seen in the midst of necrosis, and at the periphery of the abscess scattered small collections of trophozoites may be present. The separation between liver parenchyma and necrosis so clearly demarcated on gross examination is less obvious under the microscope. The surrounding liver parenchyma shows various degrees of compression as well as an infiltrate of lymphocytes and macrophages.

#### PLEUROPULMONARY AMEBIASIS

This is the second most important extraintestinal complication of amebiasis. It ranks next to liver abscess in frequency and was the second leading cause of death in amebiasis in Brandt's series.<sup>3</sup> Most cases are secondary to a transdiaphragmatic rupture of a hepatic abscess. Pulmonary and pleural amebiasis have been classified according to the route of dissemination of the ameba, a classification that serves no useful purpose. An amebic empyema will occur when a hepatic abscess ruptures into a pleural space without fibrous adhesions between the lung and the diaphragm. When the pulmonary parenchyma is involved, an abscess similar in structure to that seen in the liver may develop; however, the lesion in the lung has a more pronounced circumscribing fibroplastic reaction.

TABLE II. LOCALIZATION OF AMEBIC LESIONS IN THE BRAIN. (17 CASES)

<i>Location</i>	<i>Right</i>	<i>Left</i>	<i>Total</i>
Frontal	6	7	13
Parietal	0	3	3
Temporal	0	3	3
Occipital	2	6	8
Basal ganglia	6	11	17
Cerebellum	1	2	3
Meninges	1	5	6
Total	16	37	53

Reproduced by permission from Lombardo, L., Alonso, P., Saenz Arroyo, L., Brandt, H., and Mateos, J. H.: Cerebral amebiasis. *J. Neurosurg.* 21:704-09, 1964.

Occasionally, a liver abscess communicates with a bronchus to create a true bronchohepatic fistula. In these instances the pulmonary parenchyma may be minimally involved. Trophozoites may be found in the chocolate-colored sputum.

#### MUCOCUTANEOUS AMEBIASIS

Skin as well as extraintestinal mucosal surfaces can be infected by amebas. The involvement may result from direct extension of an intestinal lesion into the adjacent skin, i.e., from rectum to anus to perianal areas. The skin ulcers in these areas frequently elicit a condylomatous reaction which simulates either malignancy or venereal warts. Other routes of spread include spontaneous rupture of liver abscesses into the subcutaneous tissue of the abdominal wall, needle tracts following aspiration of liver abscesses, and colostomies, while direct inoculation of face and nose by soiled fingers also occurs. The typical cutaneous ulcer is deep, large, and has a necrotic base covered by an often foul-smelling yellow slough. The ulcer is rimmed by a raised erythematous border which on microscopic examination displays marked pseudoepitheliomatous hyperplasia. Amebas are found in the exudate and beneath the epidermis. The ulcers spread rapidly and can be extremely painful.

Amebiasis of the external genitalia is rare. Review of the world literature in 1976 by Thomas<sup>4</sup> uncovered only eight cases of penile amebiasis to which one was added by the author. Of these, three had a

TABLE III. EPIDEMIOLOGY PATHOGENESIS AND CLINICAL FINDINGS IN PRIMARY AMEBIC MENINGOENCEPHALITIS\*

	<i>Naegleria</i>	<i>Acanthameba</i>
Clinical history	In good health, recent history of swimming in lake or "hole"	History of poor health or immunosuppression. No history of swimming
Incubation period	4 to 7 days	Uncertain, more than 10 days
Portal of entry	Olfactory neuro-epithelium through cribriform plate into subarachnoid space.	Olfactory neuroepithelium, lungs, skin lesions, genito-urinary tract?
Onset	Rapid	Slow (up to 3 years)
Signs & symptoms	Severe headaches, parosmia, anorexia, nausea, vomiting, fever, diplopia, ataxia, coma, and death	Debilitated and chronically ill, immunosuppressed, meningeal irritation, coma, and death
Clinical course	Acute, fulminant, survival rarely exceeds a week after onset of neurological symptoms	Chronic, survival is several weeks to months after onset of neurological symptoms
Pathology	Acute ulcerative rhinitis in olfactory area, acute, purulent leptomeningitis, hemorrhagic necrotizing meningoencephalitis, cerebral edema, perivascular collection of amebas	Chronic granulomatous encephalitis with focal necrosis and multinucleated giant cells, hydrocephalus, visceral and cutaneous amebic granulomas. Perivascular collection of amebas

\*Modified from Sotelo-Avila<sup>7</sup>

history of coitus per anum, two had amebic vaginitis in their respective spouse, and three had phimosis. The penile lesion is basically a destructive, ulcerative process involving both glans and shaft. The ulcer is covered with purulent or serosanguinous material. Amebas are easily found on smears of the slough or on biopsies. The lesion in amebic vaginitis is similar to that of the perianal region. The vagina may be infected by the accidental introduction of amebas from the anal orifice, by the presence of a rectovaginal fistula, and rarely through venereal contact.

### CEREBRAL AMEBIASIS

Involvement of the brain by *E. histolytica* is rare. Review of the world literature by Lombardo<sup>5</sup> revealed that up to 1962 only 96 cases of this complication were reported. Table II, taken from the same report, shows the localizations of the lesions.

Gross examination of the brain shows variable degrees of edema and herniation depending on the number, size, and topography of the lesions. Small lesions appear as minute foci of softening with petechial hemorrhages, whereas larger and older ones become true cavities with well delineated walls filled with yellow-green necrotic material. Microscopic examination of the small lesions show poorly outlined foci of necrosis mixed with predominantly round cell inflammatory infiltrates. The circumscribing walls of the large lesions are composed of irregular layers of neuroglia surrounded by an intense astrocytic reaction.

Since 1965, following the report by Fowler,<sup>6</sup> a new form of cerebral amebiasis caused by free living amebae has been recognized. An earlier report by Derrick<sup>8</sup> in 1948 passed largely unnoticed. The amebas implicated in primary amebic meningoencephalitis belong to a large group of protozoa that inhabit brackish or fresh waters, moist soil, or decaying vegetation. Only species of the genus *Naegleria* or the *Hartmannella-Acanthameba* group are responsible for causing meningoencephalitis in man. Although infections by either of these groups are usually referred to as primary meningoencephalitis, it should be understood that they occur in different clinical settings and produce two distinct nosologic entities. Their differences and characteristics are presented in Table III.

It is very probable that the frequency of primary amebic meningoencephalitis has been underestimated. In a retrospective analysis of four cases previously diagnosed as nonspecific purulent meningitis, Napolitano<sup>9</sup> demonstrated the presence of amebas in two.

### ACKNOWLEDGMENT

Most of the slides projected during the presentation of Pathology of Amebiasis were made available by Daniel H. Connor, M.D., chief, Geographic Pathology Division, Armed Forces Institute of Pathology. I thank him for his kind and courteous cooperation.

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